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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/545,428 04/07/00 LEVESQUE M D

M CEDAR-044526

EXAMINER

HM12/0717

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SCHMIDT, M

ART UNIT

PAPER NUMBER

1635

DATE MAILED:

07/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/545,428	Applicant(s) LEVESQUE M D-ET AL.	
	Examiner Mary Schmidt	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-27 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

KATRINA TURNER
PATENT ANALYST

Attachment(s)

- | | |
|--|--|
| 15) <input type="checkbox"/> Notice of References Cited (PTO-892) | 18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____ |
| 16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 17) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ | 20) <input type="checkbox"/> Other: |

Art Unit: 1635

DETAILED ACTION

1. Claims 1-27 stand rejected under nonstatutory double patenting and under 35 U.S.C. 112.
2. It is noted that copies of the claimed foreign priority documents will be supplied by Applicant to comply with 35 U.S.C. 119 (b).

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,087,168 for the same reasons of record as set forth in the Official Action mailed 11/21/00.

It is noted that upon indication of allowable subject matter, Applicant will file a terminal disclaimer.

Art Unit: 1635

Claim Rejections - 35 USC § 112

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
6. Claims 5-12 and 15-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons of record as set forth in the Official Action mailed 11/21/00.

Applicant's arguments filed 05/02/01 (which refer the remarks filed 03/26/01) have been fully considered but they are not persuasive.

Applicant argues that "the specification discloses numerous useful examples of morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell and methods for detecting them.... the specification discloses in detail how various neural-specific antigenic markers were detected on the surfaces of transfected cells... and that only cells that, in addition to at least one neuronal antigenic marker, expressed processes 50 microns or longer were counted as neurons...." Applicant asserts that "a transdifferentiated cell in accordance with the claimed invention must have at least one morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, but uniformity of antigenic markers among the individual cells is not an essential element of the claimed invention."

Applicant then points to data in the specification to support that various combinations of antigenic

Art Unit: 1635

markers were found in cells having processes. Applicant further points to the definition of a "neuron" as defined by several criteria and cites art to teach that "different neuronal populations express a specific set of neural markers, neurotransmitters, and receptors, and that as neuronal precursor cells differentiate into other neuronal cell types in response to physiological signals in the microenvironment, the set that is expressed will be different."

In response, the written description rejection was made based on the variability known in the art for neuronal cell morphology and physiology. It was argued that one skilled in the art would not be in possession of the scope of possible "neuronal" cells claimed in view of the breadth of claimed "neuronal" cells. It was argued that the specification as filed, although it teaches expression of certain markers, does not provide a representative number of species of possible "neuronal" cells broadly encompassed by any cell expressing any neural-specific antigenic marker known in the art. Since the claimed cells are generated recombinantly, via addition of certain growth factors and antisense to reduce gene expression of certain genes, the claimed "transdifferentiated" cells would not be expected to share the same gene expression patterns as nerve cells generated naturally in a whole organism. In fact, the claimed cells initiate as differentiated epidermal cells, which would have a specific pattern of epidermal cell gene expression prior to manipulation with the nerve growth factors and antisense as taught in the specification as filed. Thus, to assert that any known nerve-antigenic marker would serve as a marker for the claimed "transdifferentiated" cells would not take into account the unique nature of the present invention, wherein the antisense to human MSX1 and human HES1 genes, coupled

Art Unit: 1635

with growth in particular nerve growth factors, results in a specific phenotype of cells as taught in the specification as filed. One skilled in the art would have no grounds for the assumption that any neuronal marker would be generated under these conditions as applied to epidermal cells, considering the unpredictability in the art as to expression patterns in different nerve cells at different stages of development and the inability to draw a specific nexus between the expression patterns in nerve cells developing naturally in a whole organism with the “neuronal” cells of the claimed invention which begin as differentiated epidermal cells.

7. Claims 1-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for differentiated cells showing some specific neuronal cell features, does not reasonably provide enablement for the scope of methods for making neuronal cells as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons of record as set forth in the Official Action mailed 11/21/00.

Applicant's arguments filed 05/02/01 (which refer the remarks filed 03/26/01) have been fully considered but they are not persuasive.

It is noted that the amendments to the claims further clarify that the negative regulators claimed are human HES1 and human MSX1 and use of other negative regulators are not claimed. It is further noted that the intent of the claimed invention is to make and use the cells in cell

Art Unit: 1635

culture, however, the claims as written do not specify *in vitro* and thus still broadly read on *in vivo* use.

In regards to the scope of claimed cells, Applicant first argues that the specification as filed teaches that “the claimed method of transdifferentiating an epidermal basal cell indeed works to transdifferentiate at least some large subset of the cell population... the identity of which is not material to enablement.” Applicant later states that “the specification teaches a method of transdifferentiation of epidermal basal cells and discloses that the further course of development of the transdifferentiated cells depends on the *in situ* environmental cues to which they are exposed. Thus, the transdifferentiated cells can be manipulated to express a set of properties (e.g., morphological or antigenic) that is characteristic of certain populations of neurons. The transdifferentiated cells may or may not express all the biochemical, morphological, physiological and functional characteristics of a given neuronal or glial cell population. For example, they may or may not form functional interneuronal connections. But regardless, they are at least useful simulations of neurons or glial cells for screening or isolating promising new drugs or neural growth factors. Once the potential of a chemical agent is identified by the claimed methods, then, of course, further research can be done to verify its actual effect on particular cell populations of the nervous system and ascertain its clinical usefulness.”

In response, the claims are drawn to transdifferentiated cells and methods of using said cells. The claims are not drawn to methods for screening for cells which produce at least one neuronal antigenic marker. Thus, to make and use the claimed invention, one skilled in the art

Art Unit: 1635

must be able to first make the claimed cells. Applicant argues that the method used to generate the transdifferentiated cells encompasses a mixed group of cells in cell culture isolated from human skin, and that the actual characterization of the cells is not important for the use of the cells to screen potential drug targets as long as the cells have at least one feature of a neuronal cell. For the reasons argued above, Examiner disagrees that Applicant would be in possession of a representative number of such transgenic cells by merely recognizing one possible antigenic marker known in the art for any possible type of neuronal cell. The specification as filed teaches that certain antigenic markers are expressed and certain phenotypes are encompassed. The claim of the specific phenotypic markers serves to identify the cells characterized by the specification as filed as "neuronal" since the art does not teach an art defined term for such dedifferentiated cells. The need to perform further basic research to characterize other such transdifferentiated cells would involve further experimentation. Since neither the art nor the specification as filed teach specific guidance as to what other possible neuronal antigenic markers would characterize the claimed cells as "neuronal", one skilled in the art would necessarily practice "trial and error" experimentation to further characterize any possible cell as transdifferentiated as broadly claimed. In view of the lack of guidance in the art, one skilled in the art would necessarily practice an undue amount of experimentation to make and use the claimed invention.

Art Unit: 1635

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader* may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
July 15, 2001


ANDREW WANG
PRIMARY EXAMINER